Furopyridines. XIX [1]. Reaction of Furo[2,3-*b*]-, -[3,2-*b*]-, -[2,3-*c*]- and -[3,2-*c*]pyridine with Acetic Anhydride

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Dedicated to the memory of Professor Nicholas Alexandrou

Acetoxylation of *N*-oxide of furo[2,3-*b*]- **2a**, -[3,2-*b*]- **2b**, -[2,3-*c*]- **2c** and -[3,2-*c*]pyridine **2d** with acetic anhydride afforded compounds substituted normally at the α- or γ-position to the ring nitrogen, **3a**, **4a**, **4b**, **3d**, **4d**, **8** and **9**, and in addition compounds substituted on the furan ring, **5a**, **6a**, **5b**, **6b**, **7b**, **5c** and **7c** which were unexpected compounds. The structures of these compounds were established from the ir, nmr and mass spectra, and x-ray crystal analysis of **5b**.

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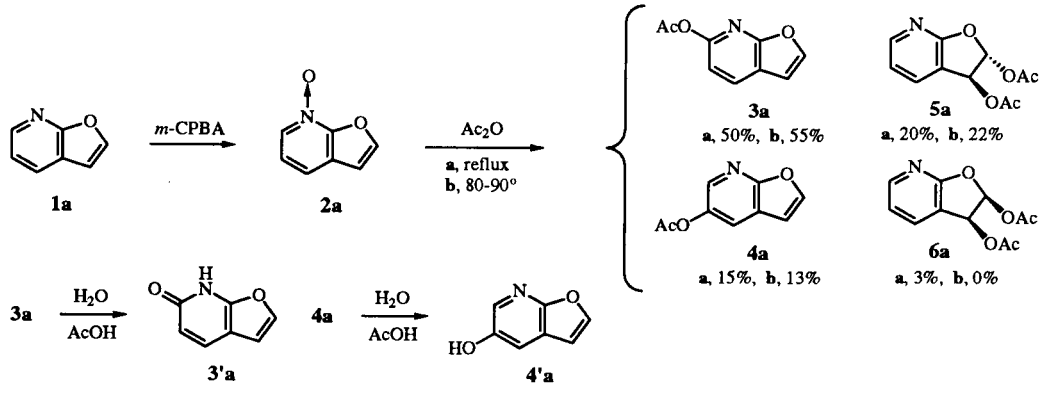
Furopyridines are of chemical and pharmacological interest because of their similarity to benzofuran, quinoline and isoquinoline which constitute an important moiety of biologically active compounds. Hitherto, we reported the syntheses of furopyridines having substituent at 2- and/or 3-position and the electrophilic reactions and lithiation which preferentially occur at the furan ring [2]. In order to extend the chemistry of furopyridines, it was desired to synthesize derivatives having substituents on the pyridine ring. For this purpose, recently we have described the cyanation, chlorination and nitration of furo[3,2-*b*]pyridine *N*-oxide [3].

It is well known that *N*-oxides of pyridine, quinoline and isoquinoline react with acetic anhydride at reflux to give an acetoxy derivative at the α-position to the ring nitrogen as the major product and the β-position to the ring nitrogen as the minor product [4]. In this paper we report the acetoxylation of furo[2,3-*b*]- **2a**, -[3,2-*b*]- **2b**, -[2,3-*c*]- **2c** and -[3,2-*c*]pyridine *N*-oxide **2d** with acetic anhydride, and the effect of the furan ring upon the acetoxylation in each annelation.

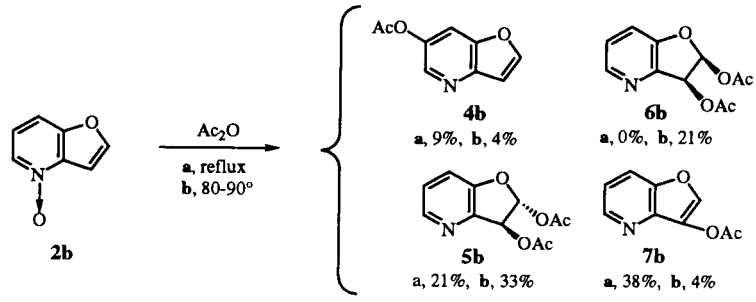
Treatment of furopyridines **1a-1d** with *m*-chloroperbenzoic acid in dichloromethane [3,5] yielded the *N*-oxides **2a-2d** in excellent yields, which were purified by distillation under reduced pressure and obtained in excellent yield as a colorless solid mass of hydrate.

Compound **2a** was refluxed with excess acetic anhydride for 1.5 hour to yield a light brown syrup from which four products, **3a** (mp 84-87.5°), **4a** (mp 92-93.5°), **5a** (bp 110-125°/0.09 mm Hg) and **6a** (bp 115-125°/0.1 mm Hg) were isolated in 50%, 15%, 20% and 3% yield, after separation by column chromatography on silica gel. The same reaction at 80-90° afforded **3a** (55%), **4a** (13%) and **5a** (22%). In the pmr spectrum, compound **3a** showed signals of the two protons of the furan ring at δ 7.68 (doublet) and 6.77 (doublet) and two protons of the pyridine at δ 7.99 (doublet) and 7.01 (doublet) (J = 8.0 Hz), from which the structure of **3a** was confirmed to be 6-acetoxyfuro[2,3-*b*]pyridine; **4a** exhibited two protons of the furan ring at δ 7.74 (doublet) and 6.78 (doublet) and two protons of the pyridine at δ 8.11 (doublet) and 7.72 (doublet) (J = 2.8 Hz), which indicated the structure as 5-acetoxyfuro[2,3-*b*]pyridine; **5a** and **6a** exhibited two aliphatic protons and two methyl protons at δ 6.69 (singlet, 1H) and 6.03 (singlet, 1H) and δ 2.13 (singlet, 3H) and 2.12 (singlet, 3H) for **5a**, and δ 6.89 (doublet, 1H) and 6.24

Scheme 1



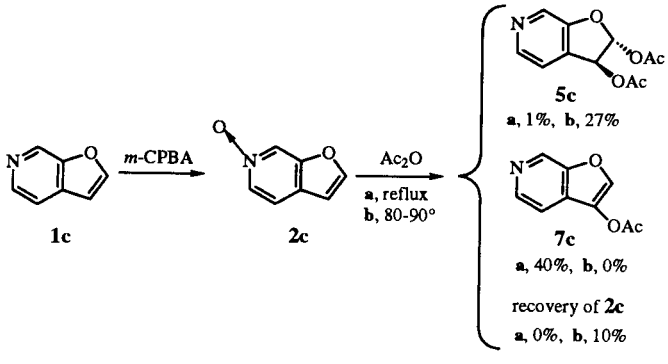
Scheme 2



(doublet, 1H) (J = 6.0 Hz) and δ 2.18 (singlet, 3H) and 2.12 (singlet, 3H) for **6a**, and three aromatic protons at δ 8.27, 7.85 and 7.02 for **5a**, and δ 8.23, 7.71 and 7.00 for **6a**. From the value of the coupling constant of the aliphatic protons the structure of **5a** was suggested to be *trans*-2,3-diacetoxy-2,3-dihydrofuro[2,3-*b*]pyridine and **6a**, *cis*-isomer. Hydrolysis of 6-acetoxy- **3a** and 5-acetoxyfuro[2,3-*b*]pyridine (**4a**) yielded the corresponding hydroxy compound (**3'a**) and (**4'a**).

The acetoxylation of **2b** at reflux yielded a brown syrup from which three compounds, **4b** (mp 106-110°), **5b** (mp 84-85.5°) and **7b** (bp 100-110°/0.15 mm Hg) were isolated in yields of 9%, 21% and 38%, respectively. The acetoxylation at 80-90° gave **4b** (4%), **5b** (33%), **6b** (mp 76.5-79°, 21%) and **7b** (4%). Compound **4b** exhibited, in its pmr spectrum, signals of two furan protons at δ 7.91 (doublet) and 7.03 (doublet) and two pyridine protons at δ 8.42 (doublet) and 7.68 (doublet, J = 2.0 Hz). Compounds **5b** and **6b** showed two aliphatic protons at δ 6.58 (doublet) and 6.11 (doublet, J = 0.8 Hz) for **5b**, and at δ 6.89 (doublet) and 6.19 (doublet) (J = 5.6 Hz) for **6b**, two methyl protons at δ 2.16 (singlet, 6H) for **5b**, and at δ 2.22 (singlet, 3H) and 2.12 (singlet, 3H) for **6b**, and three pyridine protons at δ 8.32, 7.27 and 7.27 for **5b**, and δ 8.30, 7.24 and 7.23 for **6b**, respectively. Compound **7b** showed one furan proton at δ 8.30 (singlet) and three pyridine protons at δ 8.60, 7.76 and 7.30. Thus, the structure of **4b** was suggested to be 6-acetoxyfuro[3,2-*b*]pyridine, **5b** *trans*-2,3-diacetoxy-2,3-dihydrofuro[3,2-*b*]pyridine, **6b** *cis* isomer, and **7b** 3-acetoxyfuro[3,2-*b*]pyridine.

Scheme 3



Refluxing of **2c** with acetic anhydride gave a light brown syrup, from which two products **5c** (bp 140-150°/0.08 mm Hg) and **7c** (mp 59-62°) were isolated in 1% and 40% yield, respectively. The acetoxylation at 80-90° gave compound **5c** in 27% yield accompanied by the recovery

Scheme 4

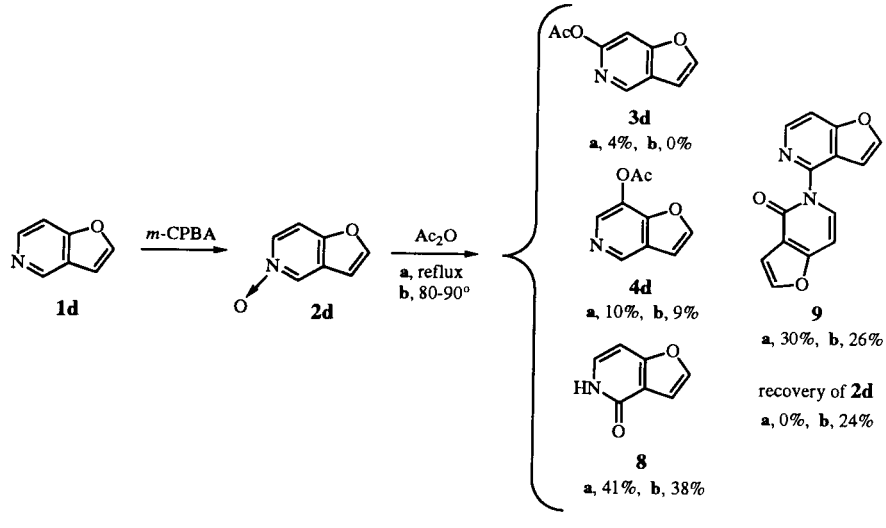


Table I

Crystal Data and Data Collection for **5b**

Formula	$C_{11}H_{11}NO_5$
Mr	237.21
Crystal system	orthorhombic
Space group	P212121
Cell constant	
a(Å)	11.748 (3)
b(Å)	25.522 (2)
c(Å)	7.792 (3)
α(°)	90.00
β(°)	90.00
γ(°)	90.00
Volume(Å^3)	2336.4 (9)
z	8
Dx, g•cm^{-3}	1.349
μ(Cu-Kα) (cm^{-1})	8.79
F(000)	992
Crystal size, mm^3	0.5 x 0.2 x 1.0
T of data collection, °C	20
Data collection method	ω-2θ scan
Scan speed in 2θ, deg•min^{-1}	12
Scan range in ω, deg	1.450+0.15tanθ
Data range measured, deg	$3 \leq 2\theta \leq 130$
Data collected	h,k,l
No. of unique data measured	2124
No. of data with $F_o > 3\sigma(F_o)$	1790
No. of variables	329
Goodness of fit	0.962
R_F	0.052
R_{wF}	0.069

Table II

Final Atomic Coordinates and Equivalent Values of Anisotropic Temperature Factors for Compound **5b** (estimated standard deviations are in parentheses)

Atom	x	y	z	Ueq
C(1)	0.9278 (5)	0.0645 (2)	0.3770 (7)	0.061 (3)
C(2)	0.8384 (5)	0.0300 (2)	0.4157 (7)	0.060 (3)
N(3)	0.7470 (4)	0.0435 (1)	0.5030 (5)	0.051 (2)
C(4)	0.7400 (4)	0.0930 (2)	0.5464 (5)	0.039 (2)
C(5)	0.8195 (3)	0.1306 (1)	0.5063 (5)	0.040 (2)
C(6)	0.9206 (4)	0.1172 (2)	0.4221 (7)	0.053 (3)
O(7)	0.7927 (2)	0.1798 (1)	0.5625 (5)	0.047 (2)
C(8)	0.6742 (4)	0.1769 (2)	0.6132 (6)	0.043 (2)
C(9)	0.6490 (4)	0.1196 (2)	0.6505 (6)	0.042 (2)
O(10)	0.6069 (3)	0.1902 (1)	0.4691 (4)	0.046 (2)
C(11)	0.5859 (4)	0.2419 (2)	0.4380 (6)	0.049 (2)
O(12)	0.6227 (4)	0.2751 (1)	0.5240 (6)	0.083 (3)
C(13)	0.5103 (5)	0.2480 (2)	0.2887 (7)	0.067 (3)
O(14)	0.6754 (3)	0.1075 (1)	0.8282 (4)	0.046 (2)
C(15)	0.5939 (5)	0.1166 (2)	0.9442 (7)	0.064 (3)
O(16)	0.5064 (4)	0.1360 (3)	0.9055 (7)	0.134 (4)
C(17)	0.6346 (7)	0.1037 (2)	1.1127 (8)	0.075 (4)

of **2c** (10%). The structures of **5c** and **7c** were confirmed from their pmr spectra: **5c** exhibited two aliphatic protons at δ 6.66 (singlet) and 6.08 (singlet) and two methyl protons at δ 2.14 (singlet, 3H) and 2.13 (singlet, 3H) and three pyridine protons at δ 8.41, 8.36 and 7.44 which suggested the structure to be *trans*-2,3-diacetoxy-2,3-dihydrofuro[2,3-*c*]pyridine, **7c** showed one furan proton at δ 8.16 and three pyridine protons at δ 8.88, 8.47 and 7.54

Table III

Bond Length in Compound **5b**

C(1) - C(2)	1.403 (8)	C(8) - C(9)	1.522 (6)
C(1) - C(6)	1.392 (7)	C(8) - O(10)	1.414 (5)
C(2) - N(3)	1.317 (6)	C(9) - O(14)	1.452 (5)
N(3) - C(4)	1.310 (6)	O(10) - C(11)	1.364 (5)
C(4) - C(5)	1.375 (6)	C(11) - 0(12)	1.164 (6)
C(4) - C(9)	1.503 (6)	C(11) - C(13)	1.472 (7)
C(5) - C(6)	1.400 (6)	O(14) - C(15)	1.336 (6)
C(5) - O(7)	1.365 (5)	C(15) - O(16)	1.181 (8)
O(7) - C(8)	1.449 (5)	C(15) - C(17)	1.506 (8)

Table IV

Bond Angles (°) in Compound **5b**

C(2) - C(1) - C(6)	120.5 (3)	C(9) - C(8) - O(10)	105.8 (2)
C(1) - C(2) - N(3)	123.9 (3)	C(4) - C(9) - C(8)	101.1 (2)
C(2) - N(3) - C(4)	115.9 (3)	C(4) - C(9) - O(14)	105.5 (2)
N(3) - C(4) - C(5)	124.9 (2)	C(8) - C(9) - O(14)	110.2 (2)
N(3) - C(4) - C(9)	128.2 (3)	C(8) - O(10) - C(11)	118.2 (3)
C(5) - C(4) - C(9)	106.9 (2)	O(10) - C(11) - O(12)	122.4 (3)
C(4) - C(5) - C(6)	120.8 (3)	O(10) - C(11) - C(13)	110.7 (3)
C(4) - C(5) - O(7)	114.3 (2)	O(12) - C(11) - C(13)	126.9 (3)
C(6) - C(5) - O(7)	124.8 (3)	C(9) - O(14) - C(15)	117.1 (3)
C(1) - C(6) - C(5)	113.9 (3)	O(14) - C(15) - O(16)	121.6 (3)
C(5) - O(7) - C(8)	105.3 (2)	O(14) - C(15) - C(17)	111.0 (3)
O(7) - C(8) - C(9)	106.6 (2)	O(16) - C(15) - C(17)	127.1 (4)
O(7) - C(8) - O(10)	108.0 (2)		

which suggested the structure to be 3-acetoxyfuro[2,3-*c*]-pyridine.

Though the structure of 2,3-diacetoxy-2,3-dihydrofuropyridines **5a**, **6a**, **5b**, **6b**, and **5c** was easily assumed by the presence of signals of two aliphatic protons and absence of the aromatic furan proton in each pmr spectrum, the configuration at C-2 and C-3 for each compound was confirmed by the X-ray crystal structure analysis of **5b** and comparison of the coupling constants between H-2 and H-3 of **5s** and **6s**.

Refluxing of **2d** with acetic anhydride gave a brown syrup from which four compounds **3d** (bp 100-120°/0.1 mm Hg), **4d** (bp 150°/0.09 mm Hg), **8** (mp 200-203°) and **9** (mp 233-235°) in yields of 4%, 10%, 41% and 30%, respectively. The acetoxylation at 80-90° afforded **4d** (9%), **8** (38%) and **9** (26%) accompanied by the recovery of **2d** (24%). In the pmr spectrum **3d** exhibited signals of two furan protons at δ 7.67 (doublet) and 6.86 (double doublet, J = 2.4, 0.8 Hz) and two pyridine protons at δ 8.68 (singlet) and 7.23 (doublet, J = 0.8 Hz). The signals of the furan proton at δ 6.86 and the pyridine proton at δ 7.23 were coupled by 0.8 Hz through a zig-zag coupling. Compound **4d** exhibited, in its pmr spectrum, signals of two furan protons at δ 7.67 (doublet) and 6.91 (doublet) and two pyridine protons at δ 8.82 and 8.33 as singlets, respectively. Thus, **3d** was assigned to 6-acetoxy- and **4d** to 7-acetoxyfuro[3,2-*c*]-pyridine. The ir and pmr spectra of compound **8** were identical with those of furo[3,2-*c*]pyridin-4(5*H*)-one reported by Eloy [6]. The elemental analysis and mass spectrum of **9** suggested the molecular formula $C_{14}H_8N_2O_3$. In the ir

Chart 1

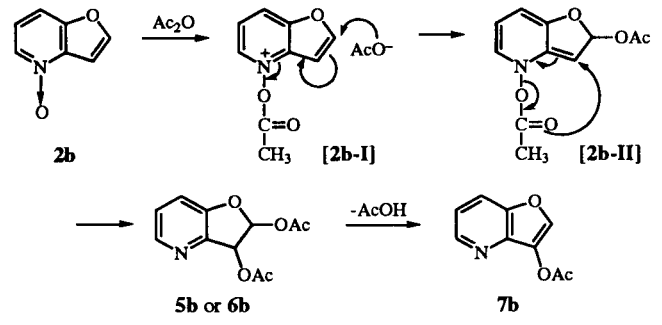


Chart 2

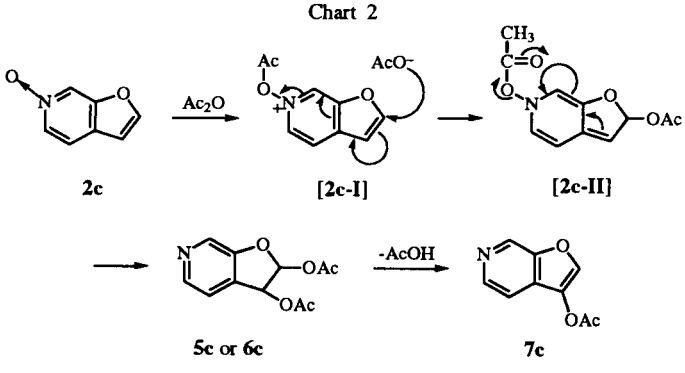
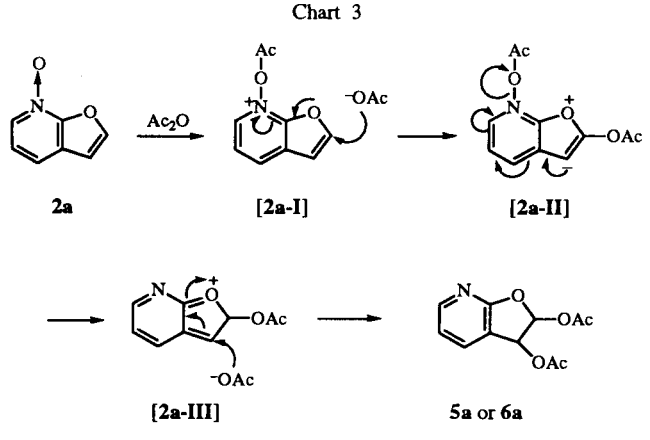


Chart 3



spectrum compound **9** exhibited a carbonyl absorption at 1690 cm^{-1}. The pmr spectrum of **9** showed two pairs of signals of furan protons at δ 7.70 (doublet, J = 2.0 Hz) and 6.81 (double doublet, J = 2.0, 0.8 Hz) and δ 7.57 (doublet, J = 2.0 Hz) and 7.06 (double doublet, J = 2.0, 1.2 Hz), and two pairs of pyridine protons at δ 7.69 (doublet, J = 8.0 Hz) and 6.72 (double doublet, J = 8.0, 0.8 Hz) and δ 8.46 (doublet, J = 5.6 Hz) and 7.55 (double doublet, J = 5.6, 1.2 Hz). The correlation of each pair was established by decoupling technique. Thus, the former pairs of the furan and pyridine protons were assigned to the furo[3,2-*c*]pyridyl part of **9**, and the latter pairs to the furo[3,2-*c*]pyridone part. The ^{13}C-nmr spectrum exhibited signals of thirteen aromatic carbons (eight methine and five quaternary carbons) and a carbonyl carbon. From these data, the structure of **9**, 5-(4'-furo[3,2-*c*]pyridyl)furo[3,2-*c*]pyridin-4(5*H*)-one, was confirmed.

Formation of compounds having an acetoxy substituent at the pyridine carbon **3a**, **4a**, **4b**, **3d** and **4d**, and furopyridone **8** and the dimeric product **9** from **2d** is interpreted by the well known mechanism for the acetoxylation of the *N*-oxides of pyridne, quinoline and isoquinoline [4]. While, formation of the 2,3-diacetoxy-2,3-dihydro compounds can be interpreted as follows, in a previous paper, we reported that the electronic effect of the pyridine ring of the furopyridines upon C-2 is exerted mainly through the C-3-C-3a bond by the comparison of ^{13}C-nmr spectral data of 2- or 3-substituted furopyridines [7]. This postulation is applicable to the interpretation for the reaction mechanism of formation of these addition products. Thus, the electron withdrawing effect of the acetoxylated nitrogen cation in the pyridine moiety of the intermediates **2b-I** and **2c-I** is efficiently exerted upon the carbon at the 2-position in furo[3,2-*b*]- and -[2,3-*c*]pyridine; that is, the resonance form having a positive charge on C-2 is possible for the intermediates from **2b** and **2c**, and impossible for **2a** and **2d**. Accordingly, in the cases of **2b** and **2c**, the first attack of the acetoxy anion occurs at C-2 to give intermediates **2b-II** and **2c-II**, and successively the second acetoxy anion attacks at C-3 followed by concerted release of the acetoxy group at the ring nitrogen (Charts 1 and 2). In the case of **2a**, the positive charge of the *N*-acetoxyammonium ion intermediate **2a-I** would directly affect the ring oxygen to form the resonance structure, and therefore the first attack of the acetoxy anion occurs at C-2 by the inductive effect of the oxonium cation to form an intermediate **2a-II**. The acetoxy group at the ring nitrogen of **2a-II** would leave through the electron transfer from the negatively charged C-3 to give the third intermediate **2a-III**. The second acetoxy anion would attack at C-3 to give compound **5a** or **6a**. The 3-acetoxyfuropyridines would be formed by elimination of the acetoxy group at C-2 and the proton at C-3 of the diacetoxy com-

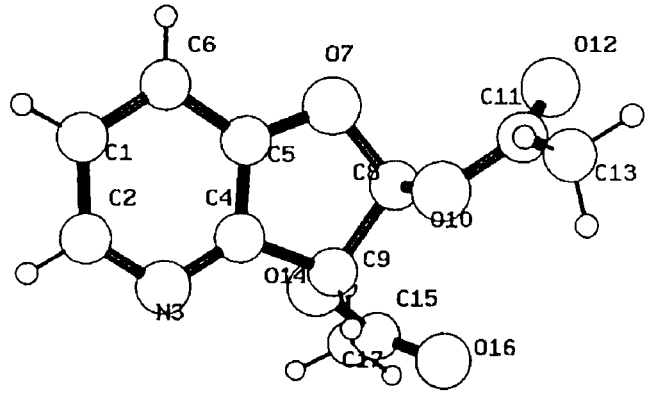


Figure 1. ORTEP drawing of compound **5b**.

pounds (Chart 3).

Thus, this research has demonstrated that the acetoxylation of *N*-oxides of furopyridines occurred not only at the pyridine ring but at the furan ring, and is significantly affected by the mode of annelation of the furopyridines.

EXPERIMENTAL

Melting points were determined by using a Yanagimoto micro melting point apparatus and are uncorrected. The ir spectra were taken on a JASCO FT/IR 7300 spectrometer. The pmr and ^{13}C-nmr spectra were recorded on a JEOL A-400 instrument with tetramethylsilane as an internal reference in deuteriochloroform. The mass spectra were obtained by using JEOL JMS-OISG-2 spectrometer.

General Procedure for the Preparation of Furo[2,3-*b*]- **2a**, Furo[2,3-*c*]- **2c** and Furo[3,2-*c*]pyridine *N*-Oxide **2d**.

A mixture of furopyridine **1a**, **1c** or **1d** (1.0 g, 8.4 mmoles) and *m*-chloroperbenzoic acid (2.5 g, purity 70%, 10.1 mmoles) in dichloromethane (25 ml) was stirred at room temperature for 22 hours. The mixture was filtered slowly through a sintered glass filter with a alumina (75 g) pad, and the filtrate was evaporated. The residual crystalline mass was recrystallized from the appropriate solvent for each *N*-oxide. Furo[3,2-*c*]pyridine *N*-oxide (**2d**) prepared by this method was identified with that of McFarland [8] by comparison of the ir and pmr spectra. Preparation of furo[3,2-*b*]pyridine *N*-oxide (**2b**) was previously reported from our laboratory [3].

Compound **2a** had mp 93.5-95° (from ether-hexane, colorless crystals); pmr: δ 8.27 (dd, J = 6.4, 1.6 Hz, 1H, H-6), 7.81 (d, J = 2.4 Hz, 1H, H-2), 7.62 (dd, J = 7.6, 1.6 Hz, 1H, H-4), 7.22 (dd, J = 7.6, 6.4 Hz, 1H, H-5), 6.95 (d, J = 2.4 Hz, 1H, H-3).

Anal. Calcd. for $C_7H_5NO_2 \cdot H_2O$: C, 54.90; H, 4.61; N, 9.15. Found: C, 54.98; H, 4.42; N, 9.13.

Compound **2c** had mp 103-103.5° (from ether-hexane, colorless crystals); pmr: δ 8.57 (dd, J = 1.6, 0.8 Hz, 1H, H-7), 8.13 (dd, J = 7.2, 1.6 Hz, 1H, H-5), 7.75 (d, J = 2.0 Hz, 1H, H-2), 7.42 (d, J = 7.2 Hz, 1H, H-4), 6.81 (dd, J = 2.0, 0.8 Hz, 1H, H-3).

Anal. Calcd. for $C_7H_5NO_2 \cdot 1/2H_2O$: C, 58.33; H, 4.20; N, 9.72. Found: C, 58.37; H, 4.27; N, 9.63.

General Procedure for the Acetoxylation of *N*-Oxides **2a-2d**.

(A) A solution of furopyridine *N*-oxide hydrate (1.51 mmoles) in acetic anhydride (2.1 ml, 22.7 mmoles) was refluxed for 1.5 hours. After evaporation of the excess acetic anhydride, the dark brown syrupy residue was treated with water, basified with sodium bicarbonate and extracted with chloroform.

(B) A solution of furopyridine *N*-oxide hydrate (2.0 mmoles) in acetic anhydride (3.0 ml, 31.6 mmoles) was heated at 90° for 1 hour. After evaporation of the excess acetic anhydride, the dark brown residue was treated with water, basified with sodium bicarbonate and extracted with chloroform. Further processing of the residue of the dried (magnesium sulfate) chloroform solution from both procedure (A) and (B) is indicated in a subsequent paragraph.

6-Acetoxy- **3a**, 5-Acetoxy- **4a**, *trans*-2,3-Diacetoxy-2,3-dihydro- **5a** and *cis*-2,3-Diacetoxy-2,3-dihydrofuro[2,3-*b*]pyridine **6a**.

The residue (310 mg) from **2a** (procedure A) was chromatographed on a silica gel (30 g) column. The first fraction eluted with chloroform-methanol (98:2) yielded 134 mg (50%) of **3a**, the second 40 mg (15%) of **4a**, the third 72 mg (20%) of **5a** and the fourth 11 mg (3%) of **6a**.

The residue (480 mg) from **2a** (procedure B) was chromatographed on a silica gel (50 g) column. The first fraction eluted with chloroform-methanol (98:2) gave 195 mg (55%) of **3a**, 46 mg (13%) of **4a** and 104 mg (22%) of **5a**.

Compound **3a**.

This compound had mp 84-87.5° (colorless crystals, from ether-hexane); ir (potassium bromide): 3149, 3125, 3093, 3042, 2925, 2870, 2845, 1751, 1598, 1533, 1462, 1408, 1303, 1276, 1208, 1161, 1116, 1023, 912, 888, 845, 748, 698 cm^{-1}; pmr: δ 7.99 (d, J = 8.0 Hz, 1H, H-4), 7.68 (d, J = 2.4 Hz, 1H, H-2), 7.01 (d, J = 8.0 Hz, 1H, H-5), 6.77 (d, J = 2.4 Hz, 1H, H-3), 2.35 (s, 3H, Me); ^{13}C-nmr: δ 169.0, 159.8, 153.5, 145.0, 132.7, 117.4, 111.7, 105.8, 20.9; ms: m/z (relative intensity) 177 (M^+,7), 136 (9), 135 (100), 107 (25), 106 (7), 79 (24), 43 (26); hrms: 177.0424 (M^+, Calcd. for $C_9H_7NO_3$: 177.0425).

Anal. Calcd. for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.30; H, 4.13; N, 7.92.

Compound **4a**.

This compound had mp 92-93.5° (colorless crystals, from ether); ir (potassium bromide): 3151, 3109, 2961, 2925, 2850, 1755, 1597, 1534, 1471, 1386, 1218, 1185, 1143, 1031, 918, 879, 802, 747 cm^{-1}; pmr: δ 8.11 (d, J = 2.8 Hz, 1H, H-6), 7.74 (d, J = 2.4 Hz, 1H, H-2), 7.72 (d, J = 2.8 Hz, 1H, H-4), 6.78 (d, J = 2.4 Hz, 1H, H-3), 2.36 (s, 3H, Me); ^{13}C-nmr: δ 169.4, 159.3, 146.3, 144.1, 137.7, 123.2, 119.6, 106.2, 21.0; ms: m/z (relative intensity) 177 (M^+, 17), 136 (9), 135 (100), 106 (5), 79 (10), 51 (12), 43 (30); hrms: 177.0426 (M^+, Calcd. for $C_9H_7NO_3$: 177.0425).

Anal. Calcd. for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.00; H, 4.12; N, 8.00.

Compound **5a**.

This compound had bp 110-125° (bath temperature, 0.09 mm Hg, colorless oil); ir (neat): 3075, 3023, 2985, 2948, 2852, 1747, 1604, 1428, 1372, 1225, 1199, 1034, 968, 884, 798 cm^{-1}; pmr: δ 8.27 (dd, J = 4.0, 2.0 Hz, 1H, H-6), 7.85 (dd, J = 7.2, 2.0 Hz, 1H, H-4), 7.02 (dd, J = 7.2, 4.0 Hz, 1H, H-5), 6.69 (s, 1H, H-2), 6.03 (s, 1H, H-3), 2.13 (s, 3H, Me), 2.12 (s, 3H, Me); ^{13}C-nmr: δ 170.1, 168.6, 167.4, 150.6, 137.0, 118.5, 116.2, 98.5, 76.1, 20.7, 20.7; ms: m/z (relative intensity) 238 (1), 237 (M^+, 1), 195 (2), 177 (30), 167 (16), 136 (14), 135 (29), 125 (31), 124 (100), 108 (17), 79 (6), 43 (99); hrms: 237.0639 (M^+, Calcd. for $C_{11}H_{11}NO_5$: 237.0636).

Anal. Calcd. for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.90. Found: C, 55.82; H, 4.85; N, 5.96.

Compound **6a**.

This compound had bp 115-125° (bath temperature, 0.1 mm Hg, colorless oil); ir (neat): 3068, 3028, 2955, 2928, 2838, 1766, 1608, 1429, 1375, 1285, 1221, 1200, 1058, 989, 965, 794 cm^{-1}; pmr: δ 8.23 (dd, J = 5.2, 1.6 Hz, 1H, H-6), 7.71 (dd, J = 7.2, 1.6 Hz, 1H, H-4), 7.00 (dd, J = 7.2, 5.2 Hz, 1H, H-5), 6.89 (d, J = 6.0 Hz, 1H, H-2), 6.24 (d, J = 6.0 Hz, 1H, H-3), 2.18 (s, 3H, Me), 2.12 (s, 3H, Me); ^{13}C-nmr: δ 170.2, 168.5, 165.5, 150.0, 135.3, 118.5, 115.9, 93.7, 71.1, 20.6, 20.3; ms: m/z (relative

intensity) 237 (M^+, 12), 177 (25), 167 (51), 166 (12), 125 (28), 124 (100); hrms: 237.0642 (M^+, Calcd. for $C_{11}H_{11}NO_5$: 237.0636).

6-Acetoxy- **4b**, *trans*-2,3-Diacetoxy-2,3-dihydro- **5b**, *cis*-2,3-Diacetoxy-2,3-dihydro- **6b** and 3-Acetoxyfuro[3,2-*b*]pyrdines **7b**.

The crude product (250 mg) from **2b** (procedure A) was chromatographed on a silica gel (30 g) column eluting with hexane-ethyl acetate (2:1) to yield 24 mg (9%) of **4b**, 75 mg (21%) of **5b** and 102 mg (38%) of **7b**.

The residue (350 mg) from **2b** (procedure B) was chromatographed on a silica gel column (40 g) eluting with hexane-ethyl acetate (2:1) to give 14 mg (4%) of **4b**, 156 mg (33%) of **5b**, 100 mg (21%) of **6b** and 14 mg (4%) of **7b**.

Compound **4b**.

This compound had mp 106-110° (colorless crystals, from ether-hexane); ir (potassium bromide): 3145, 3124, 3092, 2950, 2924, 2845, 1752, 1536, 1486, 1387, 1286, 1217, 1137, 1025, 914, 888, 788 cm^{-1}; pmr: δ 8.42 (d, J = 2.0 Hz, 1H, H-5), 7.91 (d, J = 2.4 Hz, 1H, H-2), 7.68 (dd, J = 2.4, 0.8 Hz, 1H, H-7), 7.03 (dd, J = 2.4, 0.8 Hz, 1H, H-3), 2.37 (s, 3H, Me); ^{13}C-nmr: δ 169.2, 149.9, 147.2, 145.2, 144.1, 112.5, 108.1, 21.0; ms: m/z (relative intensity) 177 (M^+, 10), 136 (7), 135 (100); hrms: 177.0420 (M^+, Calcd. for $C_9H_7NO_3$: 177.0425).

Anal. Calcd. for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.20; H, 4.35; N, 7.83.

Compound **5b**.

This compound had mp 84-85.5° (colorless crystals, from ether-hexane); ir (potassium bromide): 3105, 3085, 3038, 3003, 2931, 2877, 1744, 1584, 1435, 1232, 1155, 1040, 946, 802 cm^{-1}; pmr: δ 8.32 (dd, J = 3.6, 2.4 Hz, 1H, H-5), 7.27 (d, J = 3.6 Hz, 1H, H-6), 7.27 (d, J = 2.4 Hz, 1H, H-7), 6.58 (d, J = 0.8 Hz, 1H, H-2), 6.11 (d, J = 0.8 Hz, 1H, H-3), 2.16 (s, 6H, 2 x Me); ^{13}C-nmr: δ 170.1, 169.0, 154.1, 144.5, 144.4, 125.5, 118.3, 100.1, 76.2, 20.8, 20.7; ms: m/z (relative intensity) 237 (M^+, 4), 209 (4), 178 (5), 177 (9), 167 (49), 166 (58), 136 (17), 135 (60), 125 (58), 124 (100), 119 (8), 79 (6); hrms: 237.0645 (M^+, Calcd. for $C_{11}H_{11}NO_5$: 237 0636).

Anal. Calcd. for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.90. Found: C, 56.03; H, 4.69; N, 5.80.

Compound **6b**.

This compound had mp 76.5-79° (colorless crystals, from ether-hexane); ir (potassium bromide): 3068, 3030, 2977, 2926, 2852, 1781, 1744, 1578, 1439, 1374, 1237, 1202, 1171, 1092, 1057, 980, 965, 806 cm^{-1}; pmr: δ 8.30 (dd, J = 4.4, 2.0 Hz, 1H, H-5), 7.24 (dd, J = 8.4, 4.4 Hz, 1H, H-6), 7.23 (dd, J = 8.4, 2.0 Hz, 1H, H-7), 6.89 (d, J = 5.6 Hz, 1H, H-2), 6.19 (d, J = 5.6 Hz, 1H, H-3), 2.22 (s, 3H, Me), 2.12 (s, 3H, Me); ^{13}C-nmr: δ 170.2, 168.5, 151.9, 144.2, 144.1, 125.1, 117.9, 94.3, 71.1, 20.5, 20.2; ms: m/z (relative intensity) 237 (M^+, 8), 209 (14), 167 (90), 166 (64), 136 (23), 135 (68), 125 (100), 124 (83), 119 (20), 79 (24), 43 (61); hrms: 237.0593 (M^+, Calcd. for $C_{11}H_{11}NO_5$: 237.0636).

Anal. Calcd. for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.90. Found: C, 55.98; H, 4.58; N, 5.82.

Compound **7b**.

This compound had bp 100-110° (bath temperature, 0.15 mm Hg, colorless oil, which solidified on long standing); ir (neat): 3199, 3083, 3060, 2980, 2927, 2848, 1754, 1582, 1573, 1418, 1372, 1215, 1189, 1287, 1088, 1011, 892, 804, 771 cm^{-1}; pmr: δ 8.60 (dd, J = 4.8, 1.2 Hz, 1H, H-5), 8.30 (s, 1H, H-2), 7.76 (dd, J = 8.8, 1.2 Hz, 1H, H-7), 7.30 (dd, J = 8.8, 4.8 Hz, 1H, H-6), 2.43 (s, 3H, Me); ^{13}C-nmr: δ 167.5, 146.3, 145.7, 139.9, 137.8, 134.0, 119.9, 119.0, 20.8; ms: m/z (relative intensity) 171 (M^+, 3), 136 (8), 135 (100), 79 (28); hrms: 177.0424 (M^+, Calcd. for $C_9H_7NO_3$: 177.0425).

trans-2,3-Diacetoxy-2,3-dihydro- **5c** and 3-Acetoxyfuro[2,3-*c*]-pyridine **7c**.

The residue (200 mg) from **2c** (procedure A) was chromatographed on a silica gel (20 g) column. The first fraction eluted with chloroform-methanol (97:3) yielded 107 mg (40%) of **7c** and 4 mg (1%) of **5c**.

The residue (350 mg) from **2c** (procedure B) was chromatographed on a silica gel (40 g) column eluting with chloroform-methanol (97:3) to give 128 mg (27%) of **5c** and recovery of **2c** (24 mg, 10%).

Compound **5c**.

This compound had bp 140-150° (bath temperature, 0.08 mm Hg, colorless oil); ir (neat): 3050, 3010, 2950, 2927, 1751, 1592, 1481, 1425, 1372, 1207, 1178, 1041, 962, 873, 830 cm^{-1}; pmr: δ 8.41 (s, 1H, H-7), 8.36 (d, J = 4.8 Hz, 1H, H-5), 7.44 (d, J = 4.8 Hz, 1H, H-4), 6.66 (s, 1H, H-2), 6.08 (s, 1H, H-3), 2.14 (s, 3H, Me), 2.13 (s, 3H, Me); ^{13}C-nmr: δ 169.9, 168.9, 156.4, 143.8, 133.7, 131.4, 121.4, 100.6, 76.7, 20.7, 20.6; ms: m/z (relative intensity) 237 (M^+, 3), 195 (4), 177 (6), 167 (10), 166 (5), 136 (6), 135 (8), 125 (11), 124 (30), 79 (3), 43 (100); hrms: 237.0637 (M^+, Calcd. for $C_{11}H_{11}NO_5$: 237.0636).

Anal. Calcd. for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.90. Found: C, 55.86; H, 4.84; N, 5.82.

Compound **7c**.

This compound had mp 59-62° (from hexane, colorless crystals); ir (potassium bromide): 3145, 3100, 3075, 3050, 2925, 1751, 1563, 1427, 1364, 1219, 1182, 1097, 1086, 894, 864, 831, 820, 790 cm^{-1}; pmr: δ 8.88 (s, 1H, H-7), 8.47 (d, J = 5.4 Hz, 1H, H-5), 8.16 (s, 1H, H-2), 7.54 (d, J = 5.4 Hz, 1H, H-4), 2.40 (s, 3H, Me).

Anal. Calcd. for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.25; H, 4.10; N, 7.78.

6-Acetoxy-, **3d**, 7-Acetoxyfuro[3,2-*c*]pyridine **4d**, Furo[3,2-*c*]-pyridin-4(5*H*)one **8** and 5-(4'-Furo[3,2-*c*]pyridyl)furo[3,2-*c*]-pyridin-4(5*H*)-one **9**.

The residue (230 mg) from **2d** (procedure A) was chromatographed on a silica gel (25 g) column eluting with chloroform-methanol (97:3) to yield 11 mg (4%) of **3d**, 27 mg (10%) of **4d**, 84 mg (41%) of **8** and 57 mg (30%) of **9**.

The residue (250 mg) from **2d** (procedure B) was chromatographed on a silica gel (30 g) column eluting with chloroform-methanol (97:3) to give 32 mg (9%) of **4d**, 103 mg (38%) of **8** and 66 mg (26%) of **9**.

Compound **3d**.

This compound had bp 100-125° (bath temperature, 0.1 mm Hg, colorless oil); ir (neat): 3155, 3119, 3060, 3005, 2970, 2930, 2850, 1767, 1669, 1611, 1588, 1459, 1372, 1205, 1180, 1134, 1100, 1017, 958, 891, 748 cm^{-1}; pmr: δ 8.68 (s, 1H, H-4), 7.67

(d, J = 2.4 Hz, 1H, H-2), 7.23 (d, J = 0.8 Hz, 1H, H-7), 6.86 (dd, J = 2.4, 0.8 Hz, 1H, H-3), 2.38 (s, 3H, Me); ^{13}C-nmr: δ 169.4, 154.6, 146.2, 144.2, 141.4, 124.1, 104.9, 99.8, 21.2; ms: m/z (relative intensity) 177 (M^+, 9), 136 (8), 135 (100), 107 (31), 79 (11), 51 (17), 43 (30); hrms: 177.0421 (M^+, Calcd. for $C_9H_7NO_3$: 177.0425).

Compound **4d**.

This compound had bp 150° (bath temperature, 0.09 mm Hg, colorless oil); ir (neat): 3175, 3128, 3070, 2965, 2928, 2845, 1779, 1622, 1583, 1456, 1432, 1372, 1334, 1273, 1211, 1183, 1076, 1019, 901, 854, 753 cm^{-1}; pmr: δ 8.82 (s, 1H, H-4), 8.33 (s, 1H, H-6), 7.67 (d, J = 2.4 Hz, 1H, H-2), 6.91 (d, J = 2.4 Hz, 1H, H-3), 2.45 (s, 3H, Me); ^{13}C-nmr: δ 168.0, 150.7, 146.2, 141.9, 137.7, 132.8, 127.0, 105.3, 20.6; ms: m/z (relative intensity) 177 (M^+, 15), 136 (9), 135 (100), 79 (7), 51 (18), 43 (31); hrms: 177.0427 (M^+, Calcd. for $C_9H_7NO_3$: 177.0425).

Compound **8**.

The structure of this compound was identified by comparison of the ir and pmr spectra of the sample prepared by the method of Eloy [6].

Compound **9**.

This compound had mp 233-235° (from methanol-acetone, colorless crystals); ir (neat): 3170, 3153, 3108, 3085, 3030, 2962, 2922, 2852, 1690, 1607, 1562, 1444, 1351, 1260, 1153, 1120, 1059, 1028, 974, 841, 742, 732 cm^{-1}; pmr: δ 8.46 (d, J = 5.6 Hz, 1H, H-6'), 7.70 (d, J = 2.0 Hz, 1H, H-2), 7.69 (d, J = 8.0 Hz, 1H, H-6), 7.57 (d, J = 2.0 Hz, 1H, H-2'), 7.55 (dd, J = 5.6, 1.2 Hz, 1H, H-7'), 7.06 (dd, J = 2.0, 1.2 Hz, 1H, H-3'), 6.81 (dd, J = 2.0, 0.8 Hz, H-3), 6.72 (dd, J = 8.0, 0.8 Hz, 1H, H-7); ^{13}C-nmr: δ 160.9, 159.9, 158.5, 145.7, 143.8, 143.3, 133.7, 127.5, 121.6, 116.4, 107.9, 107.7, 106.2, 96.9; ms: m/z (relative intensity) 252 (15), 252 (M^+, 100), 195 (10); hrms: 252.0523 (M^+, Calcd. for $C_{14}H_8N_2O_3$: 252.0534).

Anal. Calcd. for $C_{14}H_8N_2O_3$: C, 66.67; H, 3.20; N, 11.11. Found: C, 66.97; H, 3.58; N, 11.34.

Hydrolysis of Compound **3a** and **4a**.

A mixture of compound **3a** (60 mg, 0.34 mmole), acetic acid (0.5 ml), ethanol (1.0 ml) and water (1.0 ml) was refluxed for 15 hours. After evaporation of the solvents, the residue was dissolved in chloroform, washed with 5% sodium bicarbonate solution, water and dried over magnesium sulfate. Evaporation of the chloroform solution gave a solid mass, which was recrystallized from acetone-hexane to yield 40 mg (87%) of furo[2,3-*b*]-pyridin-6(7*H*)-one (**3'a**).

The same procedure for **4a** (53 mg, 0.3 mmole) with acetic acid (1.5 ml), ethanol (2.0 ml) and water (2.0 ml) afforded 26 mg (64%) of furo[2,3-*b*]pyridin-5-ol (**4'a**).

Compound **3'a** had mp 179-181° (colorless crystals); ir (potassium bromide): 3200-2600 (broad), 1606, 1500, 1429, 1403, 1345, 1325, 1236, 1178, 1125, 1109, 1025, 902, 817, 743, 735 cm^{-1}; pmr: δ 12.5 (broad s, 1H, NH), 7.87 (d, J = 8.5 Hz, 1H, H-5), 7.50 (d, J = 2.4 Hz, 1H, H-2), 6.77 (d, J = 8.5 Hz, 1H, H-4), 6.69 (d, J = 2.4 Hz, 1H, H-3); ms: m/z (relative intensity) 136 (9), 135 (M^+, 100), 107 (22), 106 (14), 79 (45), 52 (38), 51 (19); hrms: 135.0318 (M^+, Calcd. for $C_7H_5NO_2$: 135.0320).

Anal. Calcd. for $C_7H_5NO_2$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.45; H, 3.83; N. 10.47.

Compound **4'a** had mp 169-171° (from acetone-hexane, colorless crystals); ir (potassium bromide): 3200-2500 (broad), 1599, 1485, 1377, 1273, 1236, 1210, 1127, 1029, 882, 798, 739 cm^{-1}; pmr: δ 8.01 (d, J = 2.8 Hz, 1H, H-6), 7.68 (d, J = 2.4 Hz, 1H, H-2), 7.44 (d, J = 2.8 Hz, 1H, H-4), 6.70 (d, J = 2.4 Hz, 1H, H-3); ms: m/z (relative intensity) 136 (8), 135 (100), 106 (11), 79 (26), 68 (11), 52 (41), 51 (24); hrms: 135.0313 (M^+, Calcd. for $C_7H_5NO_2$: 135.0320).

Anal. Calcd. for $C_7H_5NO_2$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.06; H. 3.83; N, 10.30.

X-Ray Structure Determination of Compound **5b**.

After many attempts, the structure of **5b** was finally solved by the direct method with the SHELX86 [9] and TEXSAN program [10]. Many non-H atoms were revealed on an E-map calculated by the tangent refinement method using the *E* values of 1.40-2.50 which were calculated from the observed intensities by the assistance of the atomic coordinates [11] of compound **5b** as a random group. The positional parameters of the non-H atoms were refined by full-matrix least-squares with anisotropic thermal parameters. The function minimized was $\Sigma_w(|F_o| - |F_c|)^2$, where $|F_o|$ and $|F_c|$ are the observed and calculated amplitudes of structure factors, respectively. The weighting scheme used for the final refinement was $w = 1.0/\sigma(F_o)^2$, where $\delta(F_o)^2$ is the standard deviation of each reflection intensity on the basis of counting statistics. Final R (= $\Sigma(|F_o| - |F_c|)/\Sigma|F_o|$), R_w (=$[\Sigma_w(|F_o| - |F_c|)^2/\Sigma_w(|F_o|^2]^{1/2}$), and S (=$[\Sigma_w(|F_o| - |F_c|)^2/(M-N)]^{1/2}$) are also given in Table I. None of the positional parameters for non-H atoms shifted more than their estimated standard deviations (e.s.d.s). The residual electron density in the final difference Fourier map ranged from -0.69e•Å^{-3} to 0.65e•Å^{-3}. Final positional and isotropic thermal parameters for non-H atoms are listed in Table II [12], together with their e.s.d.s in parentheses. For all crystallographic computations, the UNICS program [13] was used, and the atomic scattering factors and terms of anomalous dispersion corrections were taken from reference[13] [14].

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